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Gene Section
Short Communication

SULF2 (sulfatase 2)

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Identity

Other names: HSULF-2

HGNC (Hugo): SULF2

Location: 20q13.12

DNA/RNA

Description

SULF2 55959 chr 20: 46286150-46415360. The gene encompasses 130 kb of DNA; 21 exons.

Transcription

3 transcripts: transcript variant 1, 3909 bp linear mRNA, 21 exons (NM_018837); transcript variant 2, 4239 bp linear mRNA, 21 exons (NM_198596); transcript variant 3, 4248 bp linear mRNA, 21 exons (NM_001161841).

Protein

Description

870 amino acid; 100 kDa protein; post translational modification: 11 N-glycosylation sites; contains from N-term to C-term, a signal peptide (1-24), a enzymatic domain (25-400) which contains a conserved cysteine (88) essential for the catalytic activity, a hydrophilic domain (401-739) which contains four lysines and arginies rich domains suited for interactions with sulfated HSGAGs that fit the heparin-binding motif, and a glucosamine-6-sulfatase domain (740-870).

Expression

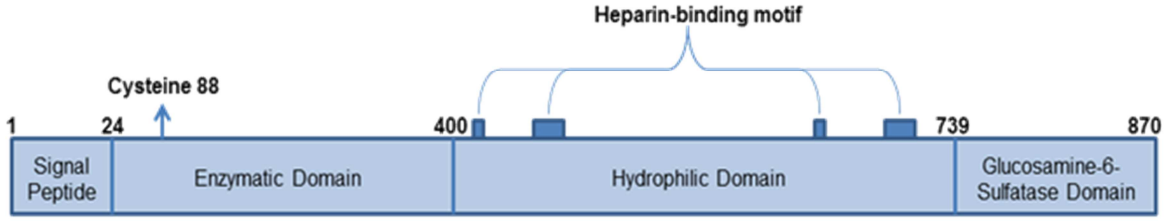
Widely expressed, especially in ovary, skeletal muscle, stomach, brain, uterus, heart, kidney, and placenta.

Localisation

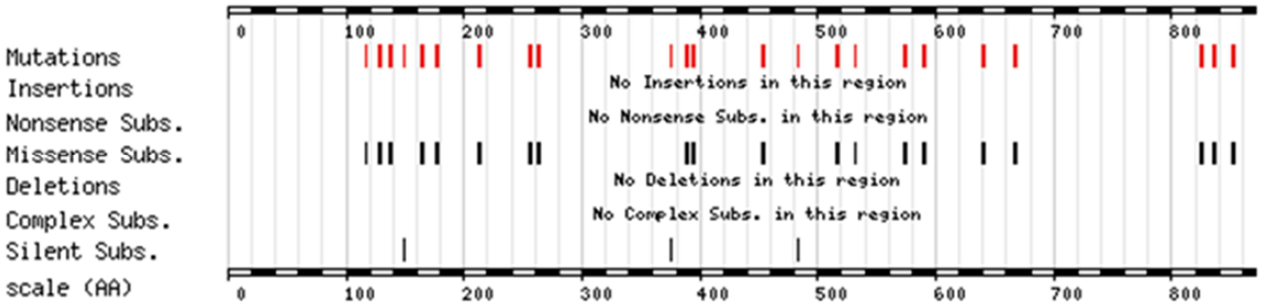
Extracellular space, cell surface, plasma membrane, endoplasmic reticulum, and Golgi stack.

Function

SULF2 is a member of a novel family of extracellular HS 6-O endosulfatases with heparin-degrading endosulfatase activity. SULF2 desulfates HS and increases the local concentration of growth factors in the extracellular matrix. The released growth factors then bind to their cell surface receptors, with the consequent activation of cell growth and survival pathways in HCC. SULF2 up-regulated GPC3 expression and FGF2 ligand-receptor binding and signaling.



Schematic diagram of SULF2 with domains.



It has been shown that SULF2 liberates growth factors such as Wnt3a from HSPGs such as GPC3 on the cell surface and in the extracellular matrix by desulfating heparan sulfate (HS).
It has been reported that SULF2 mRNA is up-regulated in human breast cancers, and suppression of SULF2 expression decreases tumorigenesis of pancreatic cancer cell lines.
SULF2 regulates PDGFRα signaling and growth in malignant glioma.

Homology

Conserved in Rhesus monkey, dog, cow, mouse, rat, chicken, and zebrafish.

Mutations

Somatic

Identified mutations in various cancers.

Implicated in

Hepatocellular carcinoma (HCC)

Prognosis

In a microarray experiment performed on paired benign and tumor tissues from HCC patients, SULF2 expression was higher in the tumors than in the benign tissues in 79 (57%) of 139 HCCs. Patients with tumors expressing high SULF2 levels had a significantly poorer prognosis than those with tumor expressing low SULF2 levels (Lai et al., 2008a).

Oncogenesis

Expression of SULF2 promotes HCC cell proliferation and migration. Knockdown of SULF2 decreases HCC cell proliferation and migration. SULF2 promotes tumorigenesis in nude mice and up-regulates GPC3 in vivo (Lai et al., 2008a).

Lung cancer

Prognosis

Paired samples of lung squamous carcinoma and non malignant neighboring tissue were obtained from 10 patients undergoing surgical resection. SULF2 increased in 8/10 pairs with a mean increase of 3 ± 0.3-fold. qPCR analysis of SULF2 in
archived cases of lung carcinoma verified it. SULF2 increased 4 ± 0.3 fold in squamous carcinomas and 3 ± 0.4 fold in adenocarcinomas (Lemjabbar-Alaoui et al., 2010).

Oncogenesis

Knockdown of SULF2 or expression of dominant-negative SULF2 reduces growth of lung cancer cells.
SULF2 over-expression in non-malignant bronchial epithelial cells induces a transformed phenotype in culture.
SULF2 knockdown reduces growth of tumors arising from lung cancer cells (Lemjabbar-Alaoui et al., 2010).

Glioblastoma (GBM)

Prognosis

SULF2 expression is elevated in GBM. Unsing a stringent cutoff of a 10-fold increase in SULF2 SAGE tags over levels in normal brain to define high SULF2 levels, 7 of 16 GBMs has increased SULF2 expression.
Strikingly, in an independent set of 424 primary human GBM tumors, SULF2 expression was increased in 46% (197/424) of tumors related to normal brain.
Immunohistochemistry on an independent set of 57 primary human GBM tumors demonstrated SULF2 protein in tumor cells in 50% of tumors.
SULF2 expression is associated with the proneural subtype of GBM characterized by abnormalities in the PDGFRα-signaling pathway and SULF2 expression is associated with the proneural GBM subtype (Phillips et al., 2012).

Oncogenesis

SULF2 confers a growth advantage to human GBM cells, SULF2 knockdown resulted in a significant decrease in cell viability.
SULF2 also confers a growth advantage to human GBM cells in vivo. SULF2 confers increased tumorigenicity and proliferation.
Prolonged survival confered by ablation of SULF2 in tumorigenic neurospheres.
And absence of SULF2 resulted in decreased tumor cell proliferation in vivo (Phillips et al., 2012).

Breakpoint number	Rearrangement type	Cytoband translocation	Breakpoint junction	Data source	Associated Genes
8	Intra-chrm translocation	20q13.13-20q13.13	51 bp insert	BAC & Cell lines	Fusion ARFGEF2-SULF2

Breakpoints

Note

Fusion of ARFGEF2 exon 1 to SULF2 exons 3-21.

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